UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: February 1, 2011

SUBJECT: Science Review of Six Mutagenicity Studies Submitted Under FIFRA 6(a)(2) for Manufacturing-Use Product *Reynoutria sachalinensis* Bioprotectant, Containing 100% *Reynoutria sachalinensis* as its Active Ingredient.

Type of Data Review:	Human Health
EPA Registration Number:	84059-1
Decision Number:	443692
DP Barcode:	385326
PC Code:	055809
CAS Number:	(none)
MRID Numbers:	48326301 thru -06
Tolerance Exemption:	40 CFR 180.1259

FROM: Gina M. Casciano, M.S., Biologist /s/ 2/1/2011
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THROUGH: Russell S. Jones, Ph.D., Senior Biologist /s/ 2/1/2011
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TO: John Fournier, Regulatory Action Leader
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ACTION REQUESTED

Marrone™ Bio Innovations, Inc., has submitted, in accordance with FIFRA Section 6(a)(2), six mutagenicity studies conducted on the active ingredient *Reynoutria sachalinensis* (Marrone's product *Reynoutria sachalinensis* Bioprotectant, EPA Reg. No. 84059-1, contains 100% *Reynoutria sachalinensis* extract as its active ingredient). Mutagenicity data requirements were waived at the time that this active ingredient was first registered (9/29/2000) and were

subsequently not required for the tolerance exemption established several years later (9/21/2005). The submitted studies (contained in MRIDs 48326301 thru -06) are being submitted at this time, per FIFRA Section 6(a)(2), because several of the studies displayed positive results for mutagenicity.

RECOMMENDATIONS AND CONCLUSIONS

The mutagenicity testing performed is **ACCEPTABLE** and supports the Agency's previous conclusion that *Reynoutria sachalinensis* extract does not present a genotoxic risk; additional data are not required.

1. The results of the Bacterial Reverse Mutation Tests (OCSPP 870.5100) displayed negative (non-mutagenic) outcomes in all strains tested except for *Salmonella typhimurim* strains TA 1537 (three studies) and TA 100 (one study). One study (MRID 48326301), showed no increased mutation frequency in any for the five bacterial strains tested. The test substance in these studies ranged from 0.25 to 100% *Reynoutria sachalinensis* as either a dry plant powder or as an ethanolic extract.

2. Both *in vivo* Mammalian Erythrocyte Micronucleus Tests (OCSPP 870.5395) performed revealed negative results (non-mutagenic) outcomes. The test substance for these studies was 100% *Reynoutria sachalinensis* extract as either a dry plant powder or an ethanolic extract.

The weight of the evidence, along with the low potential for exposure to this substance when used in accordance with label directions, supports the Agency's previous conclusion that *Reynoutria sachalinensis* extract does not present a genotoxic risk (70 FR 55275).

STUDY SUMMARIES

When first registered, mutagenicity studies were waived for the active ingredient *Reynoutria sachalinensis* because it was proposed for non-food uses only (in greenhouses on ornamental plants), with human exposure to the active ingredient anticipated to be very low when used in accordance with label instructions (i.e. low application rate, re-entry restrictions, and protective wear requirements for greenhouse workers). In addition, *Reynoutria sachalinensis* is not structurally related to a known mutagen, nor does it belong to a class of known mutagens. When food uses were proposed later (to enhance crop resistance to fungal and bacterial diseases), extract of *Reynoutria sachalinensis* was granted a tolerance exemption through Final Rule 70 FR 55272 (the BRAD was not updated to reflect this). The tolerance petition applicant requested data waivers for the following Tier I toxicology data requirements: 90–day Oral, 90–day Dermal, and 90–day Inhalation, Developmental Toxicity, and Mutagenicity. The Agency granted these

waivers based on the widespread and regular exposure that humans already have to *Reynoutria sachalinensis* in diuretic products and products for the treatment of dermatitis and athlete's foot. In addition, *Reynoutria sachalinensis* has been consumed in the human diet in Japan for generations without any known negative effects. The plant is sold commercially in Japanese supermarkets for use in soups, as a deep-fried vegetable, and as a vinegared side dish. *Reynoutria sachalinensis* is also a floral nectar source for European honey bees, and thus many more humans are already indirectly exposed to the active ingredient via consumption of honey. The Final Rule granting the tolerance exception also states that this active ingredient has been registered and used in two end-use products in Germany (Milsana fluessig and Milsana Pulver) as a resistance enhancer on fruit and vegetables since November 2000 with no reported adverse human health effects. The Final Rule does recognize the potential for a mutagenic component of the extract, emodin, to be present in product containing the active ingredient *Reynoutria sachalinensis,* however, because of the history of widespread human consumption of this plant and the probability that very little emodin would be present in the currently registered products, the Agency concluded that the use of this extract on food crops would not pose a significant dietary mutagenicity risk (70 FR 55274).

The mutagenicity studies submitted at this time (MRIDs 48326301-06) were submitted under FIFRA Section 6(a)(2) because several indicate positive results of the test substance. These studies are summarized below, followed by the reviewer's conclusions.

Bacterial Reverse Mutation Assays (MRIDs 48326301 - 48326304)

1. *Reverse Mutation Assay Using Bacteria (Salmonella typhimurim and Escherichia coli) with MBI-106-0.25* (MRID 48326301) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Bacterial Reverse Mutation Test (*Salmonella typhimurim*) OCSPP 870.5100. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The study was completed on November 10, 2010 and is Good Laboratory Practice (GLP) compliant.

   The test substance in this study was 0.25% *Reynoutria sachalinensis* as an ethanolic extract (liquid, reddish-brown in color). In the study, the test substance was investigated for its potential to induce gene mutations according to the plate incorporation test. Five bacterial tester strains were used, including: *Salmonella typhimurim* strains TA 98, TA 100, TA 1535, TA 1537 and *E. coli* strain WP2 uvrA.

   Two independent experiments were conducted, Experiment I (test substance at 0.0316, 0.100, 0.316, 1.0, 2.5 and 5.0 µL/plate) and Experiment II (test substance at 0.5, 1.0, 2.0, 3.0, 4.0 and 5.0 µL/plate). In each experiment, each level of test substance was tested in triplicate in each of the five bacterial tester strains, with and without metabolic activation (+/- S9). Incubation was for at least 48 hours at 37°C, in the dark. No precipitation of the test

substance was observed in any of the assays. No toxic effects of the test item were noted in any circumstance (i.e. not in any of the five tester strains used, at any dose, in either experiment, with and without metabolic activation).

No biologically relevant increases in revertant colonies were observed in any circumstance (i.e. not in any of the five tester strains at, any dose, in either experiment, with and without metabolic activation). The reference mutagens (i.e. positive controls) induced a distinct increase in of revertant colonies, indicating the validity of the experiments. Negative and solvent controls did not induce an increase in revertant colonies. In addition, historical laboratory control data was provided for negative control without S9 (-S9), positive control without S9 (-S9), negative control with S9 (+S9), and positive control with S9 (+S9) and confirmed that control results were within historical range.

The test substance, 0.25% *Reynoutria sachalinensis* as an ethanolic extract, is considered to be non-mutagenic in this bacterial reverse mutation assay.

2. *Reverse Mutation Assay Using Bacteria (Salmonella typhimurim and Escherichia coli) with MBI-106-20* (MRID 48326302) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Bacterial Reverse Mutation Test (*Salmonella typhimurim*) OCSPP 870.5100. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The study was completed on November 16, 2010 and is Good Laboratory Practice (GLP) compliant.

The test substance in this study was 20% *Reynoutria sachalinensis* as an ethanolic extract (liquid, reddish-brown in color). In the study, the test substance was investigated for its potential to induce gene mutations according to the plate incorporation test. Five bacterial tester strains were used, including: *Salmonella typhimurim* strains TA 98, TA 100, TA 1535, TA 1537 and *E. coli* strain WP2 uvrA.

Two independent experiments were conducted, Experiment I (test substance at 0.0316, 0.100, 0.316, 1.0, 2.5 and 5.0 µL/plate, all five bacterial strains) and Experiment II (test substance at 0.02, 0.05, 0.1, 0.2, 0.5, 1.0, 2.0 and 5.0 µL/plate for strains TA 98, TA 100, TA 1537, and WP2 uvrA and 0.01, 0.02, 0.05, 0.1, 0.2, 0.5, 1.0 and 2.0 µL/plate for strain TA 1535 only). In each experiment, each level of test substance was tested in triplicate, with and without metabolic activation (+/- S9). Incubation was for at least 48 hours at 37°C, in the dark. Precipitation of the test substance was observed in all tester strains used in Experiment I and II with and without metabolic activation. In Experiment I, precipitation of the test substance was found at a dose of 2.5 µL/plate and higher without metabolic activation and at a dose of 5.0 µL/plate with metabolic activation. In Experiment II, precipitation of the test item was found at a dose of 1.0 µL/plate and higher without metabolic activation and at a dose of 2.0 µL/plate and higher with metabolic activation.

Toxic effects of the test item were noted in both Experiment I and Experiment II in all tester strains.

- In Experiment I, toxic effects of the test item were observed at the following doses:
  - TA 98 at doses of 2.5 µL/plate and higher without metabolic activation and 5.0 µL with metabolic activation
  - TA 100 and TA 1535 at doses of 0.316 µL/plate and higher without metabolic activation and 1.0µL/plate with metabolic activation
  - TA 1537 at doses of 0.1 µL/plate higher without metabolic activation and 1.0 µL and higher with metabolic activation
- In Experiment II, toxic effects of the test item were observed at the following doses:
  - TA 98 at doses of 1.0 µL/plate and higher without metabolic activation and 5.0 µL/plate with metabolic activation
  - TA 100 at doses of 0.2 µL/plate and higher without metabolic activation and at 2.0 µL/plate and higher with metabolic activation.
  - TA 1535 at doses of 0.1 µL/plate and higher without metabolic activation and at 2.0 µL/plate and higher with metabolic activation.
  - TA 1537 at doses of 0.3 µL/plate and higher without metabolic activation and at 2.0 µL/plate and higher with metabolic activation.

Biologically relevant increase in revertant colonies was noted in test strain TA 1537 at 0.0316 µL/plate up to 0.316 µL/plate in Experiment I with metabolic activation, and at 0.1 µL/plate up to 1.0 µL/plate in Experiment II with metabolic activation. The threshold value of a 3x increase over the solvent control was exceed and a maximum mutation factor was of 7.4 was reached at a dose of 0.3 µL/plate in Experiment II with metabolic activation. No biological relevant increases were seen in any other bacterial strain in this study.

The reference mutagens induced a distinct increase in of revertant colonies, indicating the validity of the experiments. Negative and solvent controls did not induce an increase in revertant colonies. In addition, historical laboratory control data was provided for negative control without S9 (-S9), positive control without S9 (-S9), negative control with S9 (+S9), and positive control with S9 (+S9) and confirmed that control results were within historical range.

The test substance, 20% *Reynoutria sachalinensis* as an ethanolic extract, is considered to be mutagenic in this bacterial reverse mutation assay.

3. *Reverse Mutation Assay Using Bacteria (Salmonella typhimurim and Escherichia coli) with MBI-106-PP* (MRID 48326303) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Bacterial Reverse Mutation Test (*Salmonella typhimurim*) OCSPP 870.5100. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The

study was completed on November 16, 2010 and is Good Laboratory Practice (GLP) compliant.

The test substance for the study was 100% *Reynoutria sachalinensis* as dry plant powder (loose solid particles, brownish in color). In this study, the test substance was investigated for its potential to induce gene mutations according to the plate incorporation test. Five bacterial tester strains were used, including: *Salmonella typhimurim* strains TA 98, TA 100, TA 1535, TA 1537 and *E. coli* strain WP2 uvrA.

Two independent experiments (Experiments I & II) were conducted, both at the following test substance concentrations: 3.16, 10.0, 31.6, 100, 316, 1000, 2500 and 5000 µg/plate. In each experiment, each level of test substance was tested in triplicate, with and without metabolic activation (+/- S9). Incubation was for at least 48 hours at 37°C, in the dark.

Precipitation of the test substance was observed in all tester strains used in Experiment I and II with and without metabolic activation as doses of 100 µg/plate and higher with and without metabolic activation.

No toxic effects of the test item were observed in Experiments I and II in trial with metabolic activation. Toxic effects of the test item were noted in several instances in both Experiment I and Experiment II trials without metabolic activation:

- In Experiment I, toxic effects of the test item were observed at the following doses:
  - TA 100 at doses of 2500 µg/plate and higher
  - TA 1537 at a dose of 5000 µg/plate
- In Experiment II, toxic effects of the test item were observed at the following doses:
  - TA 98 at a dose of 5000 µg/plate without metabolic activation
  - TA 100 at a dose of 5000 µg/plate without metabolic activation
  - TA 1535 at a dose of 5000 µg/plate without metabolic activation
  - TA 1537 at a dose of 5000 µg/plate without metabolic activation

Biologically relevant increase in revertant colonies was noted in test strain TA 100 at a dose of 2500 µg/plate in Experiment II with metabolic activation. The threshold value of a 2x increase over the solvent control was exceeded and a maximum mutation factor of 2.2 was reached. Biologically relevant increases in revertant colony numbers were also observed in test strain TA 1537 at doses of 100 µg/plate and 316 µg/plate in Experiment II with metabolic activation. The threshold value of 3x increase over the solvent control was exceeded and a maximum mutation factor of 4.6 was reached. No biological relevant increases were seen in any other bacterial strain in this study.

The reference mutagens induced a distinct increase in of revertant colonies, indicating the validity of the experiments. Negative and solvent controls did not induce an increase in revertant colonies. In addition, historical laboratory control data was provided for negative

control without S9 (-S9), positive control without S9 (-S9), negative control with S9 (+S9), and positive control with S9 (+S9) and confirmed that control results were within historical range.

The test substance, 100% *Reynoutria sachalinensis* as dry plant powder, is considered to be mutagenic in this bacterial reverse mutation assay.

4. *Reverse Mutation Assay Using Bacteria (Salmonella typhimurim and Escherichia coli) with MBI-106-AS* (MRID 48326304) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Bacterial Reverse Mutation Test (*Salmonella typhimurim*) OCSPP 870.5100. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The study was completed on November 16, 2010 and is Good Laboratory Practice (GLP) compliant.

The test substance in this study was 100% *Reynoutria sachalinensis*, prepared as an ethanolic extract. In the study, the test substance was investigated for its potential to induce gene mutations according to the plate incorporation test. Five bacterial tester strains were used, including: *Salmonella typhimurim* strains TA 98, TA 100, TA 1535, TA 1537 and *E. coli* strain WP2 uvrA.

Two independent experiments were conducted, Experiment I (test substance at 10.0, 31.6, 100, 316, 1000, 2500 and 5000 µg/plate, all five bacterial strains) and Experiment II (test substance at 50, 100, 200, 500, 1000, 2000 and5000 µg/plate for strains TA 98, TA 100, TA 1535, and WP2 uvrA and 10, 20, 50, 100, 200, 350, 1000, 2000 and 5000 µg/plate for strain TA 1535 only). In each experiment, each level of test substance was tested in triplicate, with and without metabolic activation (+/- S9). Incubation was for at least 48 hours at 37°C, in the dark.

Precipitation of the test substance was observed in all tester strains used in Experiment I and II with and without metabolic activation. In Experiment I, precipitation of the test substance was found at a dose of 2500 µg/plate and higher with and without metabolic activation. In Experiment II, precipitation of the test item was found at a dose of 2000 µg/plate and higher with and without metabolic activation.

Toxic effects of the test item were noted in both Experiment I and Experiment II in all tester strains.

- In Experiment I, toxic effects of the test item were observed at the following doses:
  - TA 98 at doses of 2500 µg/plate and higher without metabolic activation and 5000 µg/plate with metabolic activation
  - TA 100 and TA 1537 at doses of 316 µg/plate and higher without metabolic activation and 2500 µg/plate and higher with metabolic activation

  - TA 1535 at doses of 5000 µg/plate with and without metabolic activation.
- In Experiment II, toxic effects of the test item were observed at the following doses:
  - TA 98 at doses of 2000 µg/plate and higher without metabolic activation
  - TA 100 and TA 1537 at doses of 200 µg/plate and higher without metabolic activation and 5000 µg/plate with metabolic activation
  - TA 1535 at doses of 500 µg/plate and higher without metabolic activation and at 5000 µg/plate with metabolic activation

Biologically relevant increase in revertant colonies was noted in test strain TA 1537 at 100 and 316 µg/plate in Experiment I with metabolic activation, and from doses of 20 to 200 µg/plate in Experiment II with metabolic activation. The threshold value of a 3x increase over the solvent control was exceed and a maximum mutation factor was of 4.5 was reached at a dose of 200 µg/plate in Experiment II with metabolic activation. No biological relevant increases were seen in any other bacterial strain in this study.

The reference mutagens induced a distinct increase in of revertant colonies, indicating the validity of the experiments. Negative and solvent controls did not induce an increase in revertant colonies. In addition, historical laboratory control data was provided for negative control without S9 (-S9), positive control without S9 (-S9), negative control with S9 (+S9), and positive control with S9 (+S9) and confirmed that control results were within historical range.

The test substance, 100% *Reynoutria sachalinensis* as an ethanolic extract, is considered to be mutagenic in this bacterial reverse mutation assay.

For more information, please refer to directly to MRIDs 48326301-48326304 (DERs were not prepared for these studies).

Mammalian Erythrocyte Micronucleus Assays (MRIDs 48326305 - 48326306)

1. *Mammalian Micronucleus Test of Murine Peripheral Blood Cells with MBI-106-AS* (MRID 48326305) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Mammalian erythrocyte Micronucleus Test OCSPP 870.5395. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The study was completed on December 5, 2010 and is Good Laboratory Practice (GLP) compliant.

The test substance in this study was 100% *Reynoutria sachalinensis* as an ethanolic extract. In the study, the test substance was investigated for its potential to induce micronuclei in polychromatic erythrocytes (PCE). Cottonseed oil was the vehicle (and negative control), chosen due to its relative non-toxicity to the test animals. The test animals were young,

healthy, adult mice (strain: NMRI). Following a range-finding study, the test substance concentrations set for this experiment were 250, 125, and 50 milligrams test substance per kilogram body weight (mg/kg bw). All animals treated showed signs of systemic toxicity, including reduction of spontaneous activity, constricted abdomen, piloerection, diarrhea, uncoordinated movements, half eyelid closure, eyes closed, prone position, and nasal discharge.

For all animals, including positive and negative control groups, 10,000 polychromatic erythrocytes per animal were scored at for incidence of micronucleated immature erythrocytes via blood sampling at 44 and 68 hours post treatment. The negative control animals and all dose group animals displayed an incidence of micronucleated immature erythrocytes within the historical negative control date range. No biologically relevant increase in micronuclei was found after treatment with the test item in any of the dose groups evaluated. Statistical tests (Mann-Whitney) showed no statically relevant increase in micronuclei in any dose group evaluated. The positive control (cyclophosphamide, 40 mg/kg bw) induced a significant increase in micronucleus frequency, demonstrating the validity of the assay. Therefore, the test substance, 100% *Reynoutria sachalinensis* as an ethanolic extract, is considered to be non-mutagenic with respect to clastogenicity and aneugenicity (therefore not inducting chromosomal structural damage or abnormal number of chromosomes) in this mammalian erythrocyte micronucleus test.

2. *Mammalian Micronucleus Test of Murine Peripheral Blood Cells with MBI-106-PP* (MRID 48326306) was performed by BSL Bioservice Scientific Laboratories GmbH (Behringstrasse 6/8, 82152 Planegg, Germany). The study type is: Mammalian erythrocyte Micronucleus Test OCSPP 870.5395. The sponsor and submitter of the study is Marrone Bio Innovations (2121 Second Street, Suite B-107, Davis, CA, 95618). The study was completed on December 1, 2010 and is Good Laboratory Practice (GLP) compliant.

The test substance in this study was 100% *Reynoutria sachalinensis* as dry plant powder. In the study, the test substance was investigated for its potential to induce micronuclei in polychromatic erythrocytes (PCE). Cottonseed oil was the vehicle (and negative control), chosen due to its relative non-toxicity to the test animals. The test animals were young, healthy, adult mice (strain: NMRI). Following a range-finding study, the test substance concentrations set for this experiment were 500, 250, and 125 mg/kg bw. The two lower test groups showed moderate signs of systemic toxicity. The highest test group showed signs of systemic toxicity, including reduction of spontaneous activity, constricted abdomen, diarrhea, uncoordinated movements, half eyelid and/or eye closure, prone position, and nasal discharge.

For all animals, including positive and negative control groups, 10,000 polychromatic erythrocytes per animal were scored at for incidence of micronucleated immature erythrocytes via blood sampling at 44 and 68 hours post treatment. The negative control

animals and all dose group animals displayed an incidence of micronucleated immature erythrocytes within the historical negative control date range. No biologically relevant increase in micronuclei was found after treatment with the test item in any of the dose groups evaluated. Statistical tests (Mann-Whitney) showed no statistically significant increase ($p<0.05$) of cells with micronuclei except the value observed for the 250 mg/kg bw female group. The group was significantly increased as compared to the corresponding control. However, the value was within the range of the historical negative control data, therefore the increase was not regarded as statistically significant. The positive control (cyclophosphamide, 40 mg/kg bw) induced a significant increase in micronucleus frequency, demonstrating the validity of the assay. Therefore, the test substance, 100% *Reynoutria sachalinensis* as dry plant powder, is considered to be non-mutagenic with respect to clastogenicity and aneugenicity (therefore not inducting chromosomal structural damage or abnormal number of chromosomes) in this mammalian erythrocyte micronucleus test.

For more information, please refer to MRIDs 48326305-48326306 (DERs were not prepared for these studies).

Reviewer's Conclusions

The mutagenicity studies submitted were performed according to OCSPP guidelines and the results, taken as whole from all six studies, continue to support the Agency's previous conclusion that *Reynoutria sachalinensis* is not a potential mutagen. These studies do display positive results in the Bacterial Reverse Mutation Tests (OCSPP 870.5100) *Salmonella typhimurim* strains TA 1537 (three studies) and TA 100 (one study). However, follow-up tests *in vivo* revealed negative results in both Mammalian Erythrocyte Micronucleus Tests (OCSPP 870.5395) performed; negative results were observed in *in vivo* studies using 100% *Reynoutria sachalinensis* as an ethanolic extract and 100% *Reynoutria sachalinensis* as dry plant powder.

The amount of the active ingredient *Reynoutria sachalinensis* applied, according to current pesticide product labels, is very low. Generally, products containing 5% of this active ingredient are instructed to be diluted 0.5% v/v in water. In addition, human exposure to products containing *Reynoutria sachalinensis* is mitigated by User Safety Recommendations to "wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet."

The weight of the evidence, along with the low potential for exposure to this substance when used in accordance with label directions, leads this reviewer to conclude that the mutagenicity data submitted under this action support the Agency's previous conclusion that *Reynoutria sachalinensis* extract does not present a genotoxic risk (70 FR 55275).

CLASSIFCATION: **ACCEPTABLE**; additional data are not required.

REFERENCES

70 FR 55272-7 (2005) Reynoutria Sachalinensis Extract; Exemption from the Requirement of a Tolerance. Environmental Protection Agency. Final Rule. September 21, 2005.

EPA (2000) Extract of *Reynoutria sachalinensis* (Giant Knotweed) (055809) Biopesticide Registration Action Document. U.S. Environmental Protection Agency (EPA). Issued November 2000. [Accessed January 12, 2011: http://www.epa.gov/oppbppd1/biopesticides/ingredients/tech_docs/brad_055809.html]

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